

# **Evaluation of Patients with Gastrectomy for Malignity of Anastomosis Line**

## Mide Ameliyatlı Hastaların Anostomoz Hattının Malignite Açısından Değerlendirilmesi

Anastomoz Hattının Değerlendirilmesi / Gastrectomy for Malignity of Anastomosis Line

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#### Özet

Amaç: Mide ameliyatı geçirmiş hastaların anastomoz hattından alınan biyopsilerin histopatolojik inceleme sonuçlarını malignite açısından değerlendirmeyi amaçladık. Gereç ve Yöntem: Ocak 2009 ile Aralık 2011 tarihleri arasında Konya Eğitim ve Araştırma Hastanesi Genel Cerrahi Endoskopi Ünitesinde üst gastrointestinal sistem (GİS) endoskopisi yapılan hastalardan mide ameliyatı geçirmiş 23 hastanın endoskopik bulguları ve anastomoz hattından alınan biyopsi kayıtları, Helicobacter pylori varlığı, intestinal metaplazi (İM), displazi ve kanser açısından geriye dönük olarak incelendi. Bulgular: Hastaların yaş ortalaması 63 (30-82) olup 17'si (%74) erkek, 6'sı (%26) kadındı. Bunların 15'i (%65) malign nedenle, 8'i (%35) benign nedenle mide ameliyatı geçirmişti. Ameliyattan sonra geçen süre ortalama 46 (12-144) ay idi. Ameliyatların 17'si (%74) Billroth II, 3'ü (%13) rezeksiyonsuz gastroenterestomi, 2'si (%9) total gastrektomi, 1'i (%4) Billroth I idi. Endoskopik değerlendirmede 14 (%61) hastada alkalen reflü gastrit, 6 (%26) hastada anastomoz ülseri, 2 (%9) hastada polip, 1 (%4) hastada kanser tanımlandı. Biyopsi sonuçlarının histopatolojik incelenmesinde 5 (%22) reaktif hiperplazik değişiklikler, 5 (%22) kronik aktif gastrit, 5 (%22) displazi, 3 (%13) İM, 2 (%9) kanser tespit edildi. Tartışma: Mide ameliyatlı hastalarda, ameliyattan sonra geçen süreyle paralel olarak anastomoz hattında İM ve ardından displazi görülmektedir. Endoskopi ile takip, displazi evresinde teşhisi ve uygun tedaviyi mümkiin kılacaktır

#### Anahtar Kelimeler

Cerrahi Anastomoz; Ülser; Mide Kanseri; Endoskopi

#### Abstract

Aim: We aimed at evaluating the Histopathological examination results of biopsies obtained from the anastomosis line of patients with previous gastrectomy in terms of malignancy. Material and Method: The endoscopic findings and the biopsy records obtained from the anastomosis line of 23 patients with gastrectomy history for whom upper gastrointestinal system (GIS) endoscopy was performed at the General Surgery Clinic, Endoscopy Unit of Training & Research Hospital in Konya between Jan. 2009 and Dec. 2011 were retrospectively examined for the existence of Helicobacter pylori, intestinal metaplasia (IM), dysplasia and cancer. Results: The average age of patients was 63 (range 30-82), with 17 males (74%) and 6 females (26%). 15 (65%) of these patients had undergone a gastrectomy for a malignity, and 8 (35%) for a benign reason. The time elapsed after the surgical operation was 46 (range 12-144) months in average. 17 (74%) of these surgical operations were Billroth II, 3 (13%) gastroenterostomy without resection, 2 (9%) total gastrectomy, and 1 (4%) Billroth I. Upper GIS endoscopy revealed alkaline reflux gastritis at 14 (61%) patients, anastomosis ulcer at 6 (26%) patients, polyp at 2 (9%) patients, and cancer at 1 (4%) patient. Histopathological examination of the biopsy results displayed 5 (22%) reactive hyperplasic changes, 5 (22%) chronic active gastritis, 5 (22%) dysplasia, 3 (13%) IM, and 2 (9%) cancer. Discussion: Patients with gastrectomy history develop IM in the anastomosis line in parallel with the time elapsed after surgical operation, and subsequently develop dysplasia. Monitoring with endoscopy will make diagnosis and appropriate treatment possible in the stage of dysplasia.

#### Keywords

Surgical Anastomosis; Ulcer; Gastric Cancer; Endoscopy

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#### Introduction

The most common problems in those have had gastric surgery have been defined as alkaline reflux, gastritis and the development of cancer at the anastomosis site [1]. It is claimed that premalign and malign changes take place at the anastomotic band in time, going through a process. This process starts with atrophy, goes through the stages of metaplasia and dysplasia and ends with cancer [2]. While atrophy is the loss of glands that should be there according to the sections of the stomach, metaplasia is the replacement of these glands with others. Dysplasia is intraepithelial neoplasia [3]. It is possible to reach an early diagnosis with endoscopies and biopsies performed during the stages before the development of cancer. While the 5-year survival chance is 50% in early diagnosis, it falls to 10% in the other groups. [4]. While normal gastric mucosa is seen as normal during endoscopy, damaged mucosa can be easily differentiated with endoscopy.

The purpose of our study was to evaluate the endoscopic examination findings and the Histopathologicalal examination results of the biopsies taken from the anastomosis lines of the patients who had undergone gastric surgery from the perspectives of the existence of Helicobacter pylori (HP), reflux, ulcers, intestinal metaplasia (IM), dysplasia and cancer.

#### **Material and Method**

Out of the reports of 804 patients who had undergone upper gastrointestinal system (GIS) endoscopies and biopsies between January 2009 and December 2011, at the General Surgery Clinic Endoscopy Unit of the Konya Training and Research Hospital, the files belonging to 23 patients who had been performed endoscopies after gastric surgery and had biopsies taken from the anastomosis line were examined retrospectively. Before the endoscopy and biopsy procedures, each patient had been informed about the process and his or her written consent had been obtained. The information about the reason for the gastric surgery and the date of the operation were obtained from the files. The upper GIS endoscopy had been performed by general surgery experts, after applying xylocaine for throat anesthesia, with a Fujinon esophagogastroduodenoscope. The procedure had been carried out as the examination of the esophagus, Z-line, cardia, remaining stomach, anastomosis line and distal part, and had been recorded. From the anastomosis line biopsy was taken from all patients. Biopsy materials were examined by pathologists for the presence of HP, intestinal metaplasia, dysplasia and cancer.

#### Results

The median age of the patients was 63 (30-82); 17 (74%) were male and 6 (26%) were female. 15 (65%) had gastric surgery for malign reasons, and 8 (35%) for benign reasons. 17 (74%) surgeries were Billroth II, 3 (13%), gastroenterostomy without resection, 2 (9%), total gastectomy, and 1 (4%), Billroth I. Upper GIS endoscopy determined alkaline reflux gastritis in 14 (61%) patients, anastomosis ulcers in 6 (26%) patients, polyps in 2 (9%) patients and cancer in 1 (4%) patient. The Histopathological examination of biopsy results showed 5 (22%) reactive hyperplasic changes, 5 (22%) chronic active gastritis, 5 (22%) dysplasia, 3 (13%) IM, 2 (9%) hyperplasic polyps, 2 (9%) cancers

and 1 (4%) uniform esophagus mucosa. 17 specimens were investigated for HP presence, 14 (82%) had HP(-) and 3 (18%) had HP(+).

When the biopsy results and patient characteristics were evaluated, in the patients who had undergone gastric surgery with resection, the rise in the incidence of intestinal metaplasia and dysplasia in the anastomosis line was related to the time interval after the operation (Table 1). Furthermore, dysplasia in the anastomosis line in those who had undergone gastric surgery due to benign reasons was more frequent (Table 2). Metaplasia and dysplasia were observed in the anastomosis line as premalign lesions after Billroth II surgery (Table 3). After gastric surgery with resection, the rise in the incidence of alkaline reflux gastritis (Table 4) and H. pylori (Table 5) was accompanied by the development of intestinal metaplasia and dysplasia.

#### Discussion

Stomach anastomosis cancer was first identified by Balfour in 1922 [5]. After gastrectomy, the frequency of dysplasia incidence is 4-30%, and development frequency of carcinoma is 4-6% [6]. There are different opinions on the timing of the endoscopy to be performed after gastric surgery for the early diagnosis of the possible development of cancer. In many endoscopy units, the patients to be endoscopically followed up and its frequency depends on the experience of the endoscopist. While some endoscopists recommend yearly endoscopic followup after gastrectomy, some recommend starting after three years, and others after five years [7]. Other endoscopists recommend yearly follow-ups starting five years after the operation to patients who had undergone benign gastric surgery [8;9]. In a study carried out in England, in a five-year period, the rate of stomach cancer incidence diagnosed by yearly endoscopic follow-ups was considerably higher than diagnoses reached through "open access" endoscopy [4]. In our study, endoscopic evaluation was carried out on the patients after an average of 46 months following the surgery (Table 1). In of the biopsies taken from the patients, 13% intestinal metaplasia, 22% dysplasia and 9% cancer was determined.

The type and reason of the gastric surgery also have a role in the development of stomach anastomosis line cancer. The risk of cancer development in Billroth II operations is higher than in Billroth I. This is associated with a higher frequency of duodenogastric reflux in Billroth II. Gastric stump cancer in patients who have undergone Billroth II operations is seen particularly in the anastomosis area [2]. The incidence rate of tumor development in the anastomosis area in patients who have undergone surgery for benign lesions is 1-7%, and is associated with long-term bile stimulation [10]. In our study, intestinal metaplasia and dysplasia have been observed more often in patients who have undergone surgery for benign reasons, and those who have had Billroth II surgery (Table 2 – 3).

The most frequently encountered endoscopic findings of the patients who have undergone gastric surgery are alkaline reflux gastritis, ulcers in the anastomosis line and development of malignity [1;2]. Excess bile reflux causes the formation of precancerous lesions such as metaplasia and dysplasia in the gastric mucosa [11]. In our study, the upper GIS endoscopic examination of the patients who had undergone gastric surgery identified

Table 1. Correlation between the surgery and the biopsy taken from the anastomosis line.

Histopathological characteristics	Regular Mucosa	Hyperplastic polyp	Reagent hyperplasia	Cronic inflammations	Intestinal metaplasia	Dysplasia	Cancer	Total
Number of Patients (n)	1	2	5	5	3	5	2	23
Average duration between the surgery and endoscopy (Month)	29	27	34	36	48	75	64	46

Table 2. Distribution of histopathological characteristics according to sex and surgery reasons.

Histopathological characteristics	Regular Mucosa	Hyperplastic polyp	Reagent hyperplasia	Cronic inflammations	Intestinal metaplasia	Dysplasia	Cancer	Total	
								N	%
Male	1	1	3	4	2	4	2	17	74
Female	-	1	2	1	1	1	-	6	26
Surgery for Benign Reasons	-	-	1	2	1	4	-	8	35
Surgery for Malign Reasons	1	2	4	3	2	1	2	15	65

Table 3. Comparison of the surgery and the biopsy results taken from the anastomosis line

Histopathological characteristics	Regular Mucosa	Hyperplastic polyp	Reagent hyperplasia	Cronic inflammations	Intestinal metaplasia	Dysplasia	Cancer	Total	
Surgical Technique								n	%
Billroth II.	1	2	4	4	3	3	-	17	74
Billroth I.	-	-	1	-	-	-	-	1	4
Gastroenterostomy (No resection)	-	-	-	1	-	1	1	3	13
Total gastrectomy+esophagojejunostomy	-	-	-	-	-	1	1	2	9
Total n	1	2	5	5	3	5	2	23	100
%	4	9	22	22	13	22	9	100	

Table 4. Comparison of the endoscopic findings and the biopsy results taken from the anastomosis line.

Histopathological characteristics	Regular Mucosa	Hyperplastic polyp	Reagent hyperplasia	Cronic inflammations	Intestinal metaplasia	Dysplasia	Cancer	Total	
Endoscopic Findings								N	%
Alkaline reflux gastritis	1	-	4	4	2	3	-	14	61
Ulcer on the anastomosis line	-	-	1	1	1	2	1	6	26
Polyp on the anastomosis line	-	2	-	-	-	-	-	2	9
Malign Ulcer	-	-	-	-	-	-	1	1	4
Total n	1	2	5	5	3	5	2	23	100
%	4	9	22	22	13	22	9	100	

Table 5. Distribution of the histopathological characteristics according to Presence of Helicobacter pylori.

Histopathological characteristics	Regular Mucosa	Hyperplastic polyp	Reagent hyperplasia	Cronic inflammations	Intestinal metaplasia	Dysplasia	Cancer	Total	
								N	%
Helicobacter pylori (+)	-	-	-	-	2	1	-	3	18
Helicobacter pylori (-)	-	2	4	5	1	2	-	14	82
Total	-	2	4	5	3	3	-	17	100

alkaline reflux gastritis in 14 (61%) patients, anastomosis ulcers in 6 (26%) patients, polyps in 2 (9%) patients and cancer in 1 (4%) patient (Table 4).

HP is one of the factors blamed in anastomosis area cancers [2]. It has been claimed that HP is not seen right after gastrectomy, but occurs years after the operation and increases cell proliferation, and does not exist histologically in pre-malign areas [12]. By direct effect, HP inhibits apoptosis while increasing cellular proliferation. This constitutes a significant step in carcinogenesis [13]. In our study, while the incidence of HP was not very high, it was positive in half of the patients diagnosed with metaplasia and dysplasia (Table 5).

The acceptance as natural various gastrointestinal complaints suffered from time to time by patients who have undergone

gastric surgery, and the absence of characteristic complaints are the most important factors preventing the early diagnosis of the condition. For the early diagnosis of anastomosis area cancers, all gastrointestinal complaints of patients who have undergone gastric surgery must be treated as a warning symptom for further examination and study. These patients must be regularly checked endoscopically, and national screening protocols must be developed on the subject [14;16]. Studies emphasize the increase in the risk of anastomosis area cancers developing after gastric surgery with resection parallel to the time interval after the operation [1;14;15;17]. In our study, the diagnosis of IM cases was made an average of 48 months after the operation while in dysplasia cases this interval was found to be 75 months (Table 1).

Small number of the patients, its retrospective design and that the endoscopists who performed procedures were not equally experienced were the limitations of our study.

Alkaline reflux gastritis and ulcers in the anastomosis line are frequent findings in the endoscopic examination of patients who have undergone gastric surgery. Positive results for IM and dysplasia in the histopathological examination of biopsies taken from the anastomosis line increase directly proportional to the time passed after surgery. The follow-up of these patients with upper GIS endoscopy will make the diagnosis of cancer in the anastomosis line before it develops, while it is in the dysplasia phase, and its subsequent, meticulous follow-up possible. Prospective, randomized controlled studies are needed to establish the follow-up interval.

### Competing interests

The authors declare that they have no competing interests.

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